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| Substitute for form 1449A/PTO (Modified) | | Complete if Known | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | Application Number | 10/693,252 |
| | | Filing Date | October 24, 2003 |
| | | First Named Inventor | Meade et al. / |
| | | Art Unit | 1616 |
| | | Examiner Name | To Be Assigned |
| | | Attorney Docket Number | A-68448-3 |
| Sheet | 1 | of | 6 |

| U.S. PATENT DOCUMENTS | | | | | |
|-----------------------|-----------------------|---|-----------------------------|---|---|
| Examiner Initials* | Cite No. ¹ | U.S. Patent Document Number-Kind Code ² (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| EAS | A1 | 3,919,102 | 11-11-1975 | Kühling et al. | |
| | A2 | 4,637,988 | 01-20-1987 | Hinshaw et al. | |
| | A3 | 4,647,447 | 03-01-1987 | Gries et al. | |
| | A4 | 4,678,667 | 07-07-1987 | Meares et al. | |
| | A5 | 4,822,594 | 04-18-1989 | Gibby | |
| | A6 | 4,837,169 | 06-06-1989 | Toner | |
| | A7 | 4,877,872 | 10-31-1989 | Morgan et al. | |
| | A8 | 4,885,363 | 12-05-1989 | Tweedle et al. | |
| | A9 | 5,087,440 | 02-11-1992 | Cacheris et al. | |
| | A10 | 5,095,099 | 03-10-1992 | Parkinson et al. | |
| | A11 | 5,133,956 | 07-28-1992 | Garlich et al. | |
| | A12 * | 5,135,737 | 08-04-1992 | Keana | |
| | A13 | 5,155,215 | 10-13-1992 | Ranney | |
| | A14 | 5,188,816 | 02-23-1993 | Sherry et al. | |
| | A15 | 5,219,553 | 06-15-1993 | Kraft et al. | |
| | A16 | 5,230,883 | 07-27-1993 | Komguth et al. | |
| | A17 | 5,256,395 | 10-26-1993 | Barbet et al. | |
| | A18 | 5,262,532 | 11-16-1993 | Tweedle et al. | |
| | A19 | 5,292,414 | 03-08-1994 | Sessler et al. | |
| | A20 | 5,310,539 | 05-10-1994 | Williams | |
| | A21 | 5,322,681 | 06-21-1994 | Klaveness | |
| | A22 | 5,332,567 | 07-26-1994 | Goldenberg | |
| | A23 * | 5,338,532 | 08-16-1994 | Tomalia et al. | |
| | A24 | 5,358,704 | 10-25-1994 | Desreux et al. | |
| | A25 | 5,358,705 | 10-25-1994 | Boggs et al. | |
| | A26 | 5,407,657 | 04-18-1995 | Unger et al. | |
| | A27 | 5,419,893 | 05-30-1995 | Berg et al. | |
| | A28 * | 5,428,154 | 06-27-1995 | Gansow et al. | |
| | A29 | 5,428,156 | 06-27-1995 | Mease et al. | |
| | A30 | 5,446,145 | 08-29-1995 | Love et al. | |
| | A31 | 5,466,438 | 11-14-1995 | Unger et al. | |

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|--------------------|-----------------|-----------------|--------|
| Examiner Signature | <i>Leah Sat</i> | Date Considered | 7-7-07 |
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Sheet **2** of **6**

U.S. PATENT DOCUMENTS

| Examiner Initials* | Cite No. ¹ | U.S. Patent Document Number-Kind Code ² (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|--------------------|-----------------------|---|-----------------------------|---|---|
| AAS | A32 | 5,466,439 | 11-14-1995 | Gibby et al. | |
| | A33 | 5,531,978 | 07-02-1996 | Berg et al. | |
| | A34 | 5,554,748 | 09-10-1996 | Sleving et al. | |
| | A35 | 5,565,552 | 10-15-1996 | Magda et al. | |
| | A36 | 5,622,821 | 04-22-1997 | Selvin et al. | |
| | A37 * | 5,624,901 | 04-29-1997 | Raymond et al. | |
| | A38 * | 5,648,063 | 07-15-1997 | Gries et al. | |
| | A39 | 5,672,334 | 09-30-1997 | Ranney | |
| | A40 | 5,707,605 | 01-13-1998 | Meade et al. | |
| | A41 * | 5,874,573 | 02-23-1999 | Winchell et al. | |
| | A42 * | 5,892,029 | 04-06-1999 | Raymond et al. | |
| | A43 * | 5,900,228 | 05-04-1999 | Meade et al. | |
| | A44 | 5,914,095 | 06-22-1999 | Watson | |
| | A45 | 5,955,605 | 09-21-1999 | Axworthy et al. | |
| | A46 * | 5,976,493 | 11-02-1999 | Margerum et al. | |
| | A47 | 5,980,862 | 11-09-1999 | Meade et al. | |
| | A48 * | 6,054,114 | 04-25-2000 | Lansbury et al. | |
| | A49 * | 6,120,768 | 09-19-2000 | Griffiths et al. | |
| | A50 * | 6,123,921 | 09-26-2002 | Meade et al. | |
| | A51 * | 6,348,185 B1 | 02-19-2002 | Piwnica-Worms | |
| | A52 | 6,409,990 B1 | 06-25-2002 | Vera | |
| | A53 * | 6,521,209 B1 | 02-18-2003 | Meade et al. | |
| | A54 * | 6,656,450 B2 | 12-02-2003 | Hubin et al. | |
| | A55 * | 6,673,333 B1 | 01-06-2004 | Meade et al. | |
| | A56 * | 6,709,648 B1 | 03-23-2004 | Lauffer et al. | |
| | A57 * | 6,713,045 B1 | 03-30-2004 | Meade et al. | |
| | A58 * | 6,713,046 B1 | 03-30-2004 | Meade | |
| | A59 * | 2002/0098153 A1 | 07-25-2002 | Allen et al. | |
| | A60 * | 2002/0197648 A1 | 12-26-2002 | Silva et al. | |
| | A61 * | 2003/0004236 A1 | 01-02-2003 | Meade | |
| | A62 * | 2003/0053954 A1 | 03-20-2003 | Meade et al. | |

| | | | |
|--------------------|---|-----------------|--------|
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| U.S. PATENT DOCUMENTS | | | | | |
|-----------------------|-----------------------|---|-----------------------------|---|---|
| Examiner Initials* | Cite No. ¹ | U.S. Patent Document Number-Kind Code ² (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| <i>[Signature]</i> | A63 * | 2003/0135108 A1 | 07-17-2003 | Silva et al. | |
| | A64 * | 2003/0198597 A1 | 10-23-2003 | Meade et al. | |
| | A65 | | | | |
| | A66 | | | | |

| FOREIGN PATENT DOCUMENTS | | | | | | |
|--------------------------|----------|---|-----------------------------|---|---|----------------|
| Examiner Initials* | Cite No. | Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
| <i>[Signature]</i> | B1 | CA 2139374 | 07-01-1995 | Meyer et al. | | |
| | B2 | CA 2182686 | 08-10-1995 | Schering Aktiengesellschaft | | |
| | B3 | CA 2197074 | 02-22-1996 | Schering Aktiengesellschaft | | |
| | B4 | WO 90/12050 A1 | 10-18-1990 | Salutar, Inc. | | |
| | B5 | WO 92/19284 A1 | 11-12-1992 | University of New Mexico | | |
| | B6 | WO 94/03271 A1 | 02-17-1994 | Smith-Kline Beecham PLC | | |
| | B7 | WO 94/04485 A1 | 03-03-1994 | Mallinckrodt Medical Inc. | | |
| | B8 | WO 95/10217 A2, A3 | 04-20-1995 | Mallinckrodt Medical Inc. | | |
| | B9 | WO 95/19185 A1 | 07-20-1995 | Mallinckrodt Medical Inc. | | |
| | B10 | WO 95/19347 A1 | 07-20-1995 | Mallinckrodt Medical Inc. | | |
| | B11 | WO 95/20353 A1 | 08-03-1995 | Mallinckrodt Medical Inc. | | |
| | B12 | WO 95/27705 A1 | 10-19-1995 | Bracco International | | |
| | B13 | WO 95/28966 A1 | 11-02-1995 | Nycomed Imaging | | |
| | B14 | WO 95/31444 A1 | 11-23-1995 | Bracco International | | |
| | B15 | WO 95/32741 A1 | 12-07-1995 | Dibra S.P.A. | | |
| | B16 | WO 96/05167 A1 | 02-22-1996 | Schering Aktiengesellschaft | | |
| | B17 | WO 96/23526 A2, A3 | 08-08-1996 | Metasyn, Inc. | | |
| | B18 | WO 96/38184 A2, A3 | 12-05-1996 | California Institute of Technology | | |
| | B19 * | WO 97/00245 A1 | 01-03-1997 | Regents of University of California | | |
| | B20 | WO 97/01360 A3 | 01-16-1997 | Concat, Ltd. | | |

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| FOREIGN PATENT DOCUMENTS | | | | | | |
|--------------------------|----------|--|--------------------------------|---|---|----------------|
| Examiner Initials* | Cite No. | Foreign Patent Document Country Code ¹ Number ² Kind Code ³ (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁴ |
| [Signature] | B21 | WO 97/21431 A1 | 06-19-1997 | California Institute of Technology | | |
| | B22 | WO 97/32862 A1 | 09-12-1997 | Bracco S.P.A. | | |
| | B23 | WO 97/36619 A2,A3 | 10-09-1997 | Epix Medical, Inc. | | |
| | B24 | WO 99/21592 A1 | 05-06-1999 | California Institute of Technology | | |
| | B25 | WO 99/25389 A2 | 05-27-1999 | Research Corporation Technologies | | |
| | B26 | WO 99/59640 A2, A3 | 11-25-1999 | Bracco International B.V. | | |
| | B27 | WO 01/08712 A2, A3 | 02-08-2001 | Epix Medical, Inc. | | |
| | B28 | WO 01/52906 A2, A3 | 07-26-2001 | Epix Medical, Inc. | | |
| | B29 | WO 01/82795 A2, A3 | 11-08-2001 | Research Corporation Technologies | | |
| | B30 | WO 02/056670 A2 ✓ | 07-25-2002 | The General Hospital | | |
| | B31 | | | | | |
| | B32 | | | | | |

| NON PATENT LITERATURE DOCUMENTS | | | |
|---|-----------------------|---|--|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | |
|  | C1 | AGUAYO et al., "Nuclear magnetic resonance imaging of a single cell," Nature, Letters to Nature, 07-10-1986, 322:190-191. | |
| | C2 | ALEXANDER, "Design and Synthesis of Macrocyclic Ligands and Their Complexes of Lanthanides and Actinides," Chemical Review, 1995, 95:273-342. | |
| | C3 | BORCH, R.F., et al., "The Cyanohydridoborate Anion as a Selective Reducing Agent," Journal of the American Chemical Society, 06-1971, 93(12):2897-2904. | |
| | C4 | CHO, Z.H., et al., "Some Experiences on a 4μm NMR Microscopy," Book of Abstracts, Vol. 1, p.233, Society of Magnetic Resonance in Medicine, 6th Annual Meeting and Exhibition, August 17-21, 1987, New York City, NY., 08-1987, 1:233. | |
| | C5 | COHEN, S.M, et al., "Synthesis and Relaxation Properties of Mixed Gadolinium Hydroxypyridinonate MRI Contrast Agents, Inorganic Chemistry, 2000, 39:5747-5756. | |
| | C6 | GRYNKIEWICZ, G., et al., "A New Generation of Ca ²⁺ Indicators with Greatly Improved Fluorescence Properties," The Journal of Biological Chemistry, 1985, 260(6):3440-3450. | |
| | C7 | HENNESSY, M.J., et al., "NMR Surface Coil Microscopy," Book of Abstracts, Vol. 2, p.461-462, Society of Magnetic Resonance in Medicine, 5th Annual Meeting and Exhibition, August 19-22, 1986, Montreal, Quebec, Canada., 08-1986, 2:461-462. | |

| | | | |
|--------------------|-------------|-----------------|--------|
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| HJS | C8 | HOULT, D.I., et al., "The Signal-to-Noise Ratio of the Nuclear Magnetic Resonance Experiment," Journal of Magnetic Resonance, 1976, 24:71-85. | | |
| | C9 | HUBIN et al., "Ultra rigid cross-bridged tetraazamacrocycles as ligands- the challenge and the solution," Chemical Communications, 1998, :1675-1676. | | |
| | C10 | HUBIN et al., "Crystallographic Characterization of Stepwise Changes in Ligand Conformations as Their Internal Topology Changes and Two Novel Cross-Bridged Tetraazamacrocyclic Copper(II) Complexes," Inorganic Chemistry, 1999, 38:4435-4446. | | |
| | C11 | HUBIN et al., "New Iron(II) and Manganese(II) Complexes of Two Ultra-Rigid, Cross-Bridged Tetraazamacrocycles for Catalysis and Biomimicry," Journal of the American Chemical Society, 2000, 122:2515-2522. | | |
| | C12 | HUBIN et al., "Topologically Constrained Manganese(III) and Iron(III) Complexes of Two Cross-Bridged Tetraazamacrocycles," Inorganic Chemistry, 2001, 40:435-444. | | |
| | C13 | HUBIN et al., "Potentiometric Titrations and Nickel(II) Complexes of Four Topologically Constrained Tetraazamacrocycles," Supramolecular Chemistry, 2001, 13:261-276. | | |
| | C14 | JACKELS, "Enhancement Agents for Magnetic Resonance and Ultrasound Imaging. Chapter 20: Enhancement Agents for Magnetic Resonance Imaging: Fundamentals," Pharm. Med. Imag., 1990, 20(3):645-661. | | |
| | C15 | JACOBS et al., "Magnetic Resonance Microscopy of Embryonic Cell Lineages and Movements," Science, 1994, 263:681-684. | | |
| | C16 | JOHNSON, G.A., et al., "MR Microscopy at 7.0 T," Works in Progress, Society of Magnetic Resonance in Medicine, Sixth Annual Meeting and Exhibition, August 17-21, 1987, New York City, NY, 08-1987, :23. | | |
| | C17 | LI et al., "A Calcium-Sensitive Magnetic Resonance Imaging Contrast Agent," Journal of the American Chemical Society, 1999, 121:1413-1414. | | |
| | C18 | MEADE, T.J. et al., "Hydrophobic, Regiospecific Guest Binding by Transition-Metal Host Complexes Having Permanent Voids as Revealed by FT-NMR Relaxation Studies," Journal of the American Chemical Society, 1986, 108:1954-1962. | | |
| | C19 | MEYER et al., "Advances in Macrocyclic Gadolinium Complexes as Magnetic Resonance Imaging Contrast Agents," Investigative Radiology, 09-1990, 25(1):S53-S55. | | |
| | C20 | MOATS et al., "A "Smart" Magnetic Resonance Imaging Agent That Reports on Specific Enzymatic Activity," Agnew Chemical International Edition England, 04-1997, 36(7):726-728. | | |
| | C21 | MOI, M.K., et al., "The Peptide Way to Macrocyclic Bifunctional Chelating Agents: Synthesis of 2- (p-Nitrobenzyl) - 1,4,7,10-tetraazacyclododecan- N, N', N'', N'''- tetraacetic Acid and Study of Its Yttrium(III) Complex," Journal of the American Chemical Society, 1988, 110(18):6266-6267. | | |
| | C22 | NIJHOF, E.J., et al., "High-Resolution Proton Imaging at 4.7 Tesla," Proceedings of Soc. Magn. Reson. Med., 1987, pg. 925. | | |
| | C23 | RUNGE, V.M., et al., "Future directions in magnetic resonance contrast media," Topics in Magnetic Resonance Imaging, 1991, 3(2):85-97. | | |
| | C24 | RUSSELL, E.J., et al., "Multicenter Double-Blind Placebo-Controlled Study of Gadopentetate Dimeglumine as an MR Contrast Agent: Evaluation in Patients with Cerebral Lesions," American Journal of Roentgenology, 04-1989, 152:813-823. | | |

| | | | |
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| | | | | Filing Date | October 24, 2003 |
| | | | | First Named Inventor | Meade et al. |
| | | | | Art Unit | 1616 |
| | | | | Examiner Name | To Be Assigned |
| Sheet | 6 | of | 6 | Attorney Docket Number | A-68448-3 |

| NON PATENT LITERATURE DOCUMENTS | | | |
|---------------------------------|-----------------------|---|----------------|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ² |
| [Signature] | C25 | SHUKLA et al., "Design of Conformationally Rigid Dimeric MRI Agents," Magnetic Resonance in Medicine, 1996, 36(6):925-931. | |
| | C26 | SILLERUD, L.O., et al., "Proton NMR Microscopy of Intact Multicellular Tumor Spheroids," Book of Abstracts, Vol. 1, p.468, Society of Magnetic Resonance in Medicine, 6th Annual Meeting and Exhibition, August 17-21, 1987, New York City, NY, 08-1987, 1:468. | |
| | C27 | STAUBLI et al., "The Design and Synthesis of Fluorescently Detectable Magnetic Resonance imaging Agents for Embryonic Cell Lineage Analysis," American Chemical Society: Division of Inorganic Chemistry, 209th ACS National Meeting, Anaheim, California. Abstract No. 385 (April 2-6, 1995), 04-1995. | |
| | C28 | TSIEN, R.Y. "New Calcium Indicators and Buffers with High Selectivity Against Magnesium and Protons: Design, Synthesis, and Properties of Prototype Structures," Biochemistry, 1980, 19(11):2396-2404. | |
| | C29 | TWEEDLE, M.F., et al., "Considerations Involving Paramagnetic Coordination Compounds as Useful NMR Contrast Agents," Nuclear Medicine and Biology, 1988, 15(1):31-38. | |
| | C30 | WEISMAN et al., "Cross-Bridged Cyclam. Protonation and Li ⁺ Complexation in a Diamond-Lattice Cleft," Journal of the American Chemical Society, 1990, 112:8604-8605. | |
| | C31 | WEISMAN et al., "Synthesis and transition-metal complexes of new cross-bridged tetraamine ligands," Chemical Communications, 1996, pp. 947-948. | |
| | C32 | WONG et al., "Synthesis and Characterization of Cross-Bridged Cyclams and Pendant-Armed Derivatives and Structural Studies of Their Copper(II) Complexes," Journal of the American Chemical Society, 2000, 122:10561-10572. | |
| | C33 | | |
| | C34 | | |
| | C35 | | |
| | C36 | | |
| | C37 | | |
| | C38 | | |
| | C39 | | |

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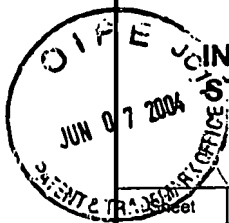
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| | | Art Unit | 1616 |
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| | | Attorney Docket Number | A-68448-3 |

| U.S. PATENT DOCUMENTS | | | | | |
|-----------------------|----------|--|--------------------------------|---|---|
| Examiner Initials* | Cite No. | U.S. Patent Document Number-Kind Code* (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | A1 | 3,919,102 | 11-11-1975 | Kühling et al. | |
| | A2 | 4,637,988 | 01-20-1987 | Hinshaw et al. | |
| | A3 | 4,647,447 | 03-01-1987 | Gries et al. | |
| | A4 | 4,678,667 | 07-07-1987 | Meares et al. | |
| | A5 | 4,822,594 | 04-18-1989 | Gibby | |
| | A6 | 4,837,169 | 06-06-1989 | Toner | |
| | A7 | 4,877,872 | 10-31-1989 | Morgan et al. | |
| | A8 | 4,885,363 | 12-05-1989 | Tweedle et al. | |
| | A9 | 5,087,440 | 02-11-1992 | Cacheris et al. | |
| | A10 | 5,095,099 | 03-10-1992 | Parkinson et al. | |
| | A11 | 5,133,956 | 07-28-1992 | Garlich et al. | |
| | A12 * | 5,135,737 | 08-04-1992 | Keana | |
| | A13 | 5,155,215 | 10-13-1992 | Ranney | |
| | A14 | 5,188,816 | 02-23-1993 | Sherry et al. | |
| | A15 | 5,219,553 | 06-15-1993 | Kraft et al. | |
| | A16 | 5,230,883 | 07-27-1993 | Komguth et al. | |
| | A17 | 5,256,395 | 10-26-1993 | Barbet et al. | |
| | A18 | 5,262,532 | 11-16-1993 | Tweedle et al. | |
| | A19 | 5,292,414 | 03-08-1994 | Sessler et al. | |
| | A20 | 5,310,539 | 05-10-1994 | Williams | |
| | A21 | 5,322,681 | 06-21-1994 | Klaveness | |
| | A22 | 5,332,567 | 07-26-1994 | Goldenberg | |
| | A23 * | 5,338,532 | 08-16-1994 | Tomalia et al. | |
| | A24 | 5,358,704 | 10-25-1994 | Desreux et al. | |
| | A25 | 5,358,705 | 10-25-1994 | Boggs et al. | |
| | A26 | 5,407,657 | 04-18-1995 | Unger et al. | |
| | A27 | 5,419,893 | 05-30-1995 | Berg et al. | |
| | A28 * | 5,428,154 | 06-27-1995 | Gansow et al. | |
| | A29 | 5,428,156 | 06-27-1995 | Mease et al. | |
| | A30 | 5,446,145 | 08-29-1995 | Love et al. | |
| | A31 | 5,466,438 | 11-14-1995 | Unger et al. | |

| | |
|--------------------|--|
| Examiner Signature | Date Considered 7-707 |
|--------------------|--|

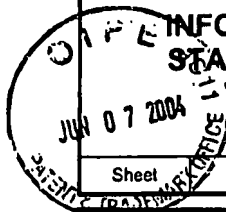
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Sheet **2** of **6**

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| First Named Inventor | Meade et al. |
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U.S. PATENT DOCUMENTS

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|--------------------|-----------------------|---|-----------------------------|---|---|
| | A32 | 5,466,439 | 11-14-1995 | Gibby et al. | |
| | A33 | 5,531,978 | 07-02-1996 | Berg et al. | |
| | A34 | 5,554,748 | 09-10-1996 | Sleving et al. | |
| | A35 | 5,565,552 | 10-15-1996 | Magda et al. | |
| | A36 | 5,622,821 | 04-22-1997 | Selvin et al. | |
| | A37 * | 5,624,901 | 04-29-1997 | Raymond et al. | |
| | A38 * | 5,648,063 | 07-15-1997 | Gries et al. | |
| | A39 | 5,672,334 | 09-30-1997 | Ranney | |
| | A40 | 5,707,605 | 01-13-1998 | Meade et al. | |
| | A41 * | 5,874,573 | 02-23-1999 | Winchell et al. | |
| | A42 * | 5,892,029 | 04-06-1999 | Raymond et al. | |
| | A43 * | 5,900,228 | 05-04-1999 | Meade et al. | |
| | A44 | 5,914,095 | 06-22-1999 | Watson | |
| | A45 | 5,955,605 | 09-21-1999 | Axworthy et al. | |
| | A46 * | 5,976,493 | 11-02-1999 | Margerum et al. | |
| | A47 | 5,980,862 | 11-09-1999 | Meade et al. | |
| | A48 * | 6,054,114 | 04-25-2000 | Lansbury et al. | |
| | A49 * | 6,120,768 | 09-19-2000 | Griffiths et al. | |
| | A50 * | 6,123,921 | 09-26-2002 | Meade et al. | |
| | A51 * | 6,348,185 B1 | 02-19-2002 | Plwnica-Worms | |
| | A52 | 6,409,990 B1 | 06-25-2002 | Vera | |
| | A53 * | 6,521,209 B1 | 02-18-2003 | Meade et al. | |
| | A54 * | 6,656,450 B2 | 12-02-2003 | Hubin et al. | |
| | A55 * | 6,673,333 B1 | 01-06-2004 | Meade et al. | |
| | A56 * | 6,709,646 B1 | 03-23-2004 | Lauffer et al. | |
| | A57 * | 6,713,045 B1 | 03-30-2004 | Meade et al. | |
| | A58 * | 6,713,046 B1 | 03-30-2004 | Meade | |
| | A59 * | 2002/0098153 A1 | 07-25-2002 | Allen et al. | |
| | A60 * | 2002/0197648 A1 | 12-26-2002 | Silva et al. | |
| | A61 * | 2003/0004236 A1 | 01-02-2003 | Meade | |
| | A62 * | 2003/0053954 A1 | 03-20-2003 | Meade et al. | |

| | | | |
|--------------------|--|-----------------|--------|
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| | | | | | Filing Date October 24, 2003 |
| | | | | | First Named Inventor Meade et al. |
| | | | | | Art Unit 1616 |
| | | | | | Examiner Name To Be Assigned |
| | | | | | Attorney Docket Number A-68448-3 |

| U.S. PATENT DOCUMENTS | | | | | |
|-----------------------|-----------------------|---|-----------------------------|---|---|
| Examiner Initials* | Cite No. ¹ | U.S. Patent Document Number-Kind Code ² (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | A63 * | 2003/0135108 A1 | 07-17-2003 | Silva et al. | |
| | A64 * | 2003/0198597 A1 | 10-23-2003 | Meade et al. | |
| | A65 | | | | |
| | A66 | | | | |

| FOREIGN PATENT DOCUMENTS | | | | | | |
|--------------------------|----------|---|-----------------------------|---|---|----------------|
| Examiner Initials* | Cite No. | Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
| | B1 | CA 2139374 | 07-01-1995 | Meyer et al. | | |
| | B2 | CA 2182686 | 08-10-1995 | Schering Aktiengesellschaft | | |
| | B3 | CA 2197074 | 02-22-1996 | Schering Aktiengesellschaft | | |
| | B4 | WO 90/12050 A1 | 10-18-1990 | Salutar, Inc. | | |
| | B5 | WO 92/19264 A1 | 11-12-1992 | University of New Mexico | | |
| | B6 | WO 94/03271 A1 | 02-17-1994 | Smith-Kline Beecham PLC | | |
| | B7 | WO 94/04485 A1 | 03-03-1994 | Mallinckrodt Medical Inc. | | |
| | B8 | WO 95/10217 A2, A3 | 04-20-1995 | Mallinckrodt Medical Inc. | | |
| | B9 | WO 95/19185 A1 | 07-20-1995 | Mallinckrodt Medical Inc. | | |
| | B10 | WO 95/19347 A1 | 07-20-1995 | Mallinckrodt Medical Inc. | | |
| | B11 | WO 95/20353 A1 | 08-03-1995 | Mallinckrodt Medical Inc. | | |
| | B12 | WO 95/27705 A1 | 10-19-1995 | Bracco International | | |
| | B13 | WO 95/28966 A1 | 11-02-1995 | Nycomed Imaging | | |
| | B14 | WO 95/31444 A1 | 11-23-1995 | Bracco International | | |
| | B15 | WO 95/32741 A1 | 12-07-1995 | Dibra S.P.A. | | |
| | B16 | WO 96/05167 A1 | 02-22-1996 | Schering Aktiengesellschaft | | |
| | B17 | WO 96/23526 A2,A3 | 08-08-1996 | Metasyn, Inc. | | |
| | B18 | WO 96/38184 A2,A3 | 12-05-1996 | California Institute of Technology | | |
| | B19 * | WO 97/00245 A1 | 01-03-1997 | Regents of University of California | | |
| | B20 | WO 97/01360 A3 | 01-16-1997 | Concat, Ltd. | | |

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| | 7-7-07 |

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| FOREIGN PATENT DOCUMENTS | | | | | | |
|--------------------------|----------|--|--------------------------------|---|---|----------------|
| Examiner Initials* | Cite No. | Foreign Patent Document Country Code ¹ Number ² Kind Code ³ (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁴ |
| | B21 | WO 97/21431 A1 | 06-19-1997 | California Institute of Technology | | |
| | B22 | WO 97/32862 A1 | 09-12-1997 | Bracco S.P.A. | | |
| | B23 | WO 97/36619 A2, A3 | 10-09-1997 | Epix Medical, Inc. | | |
| | B24 | WO 99/21592 A1 | 05-06-1999 | California Institute of Technology | | |
| | B25 | WO 99/25389 A2 | 05-27-1999 | Research Corporation Technologies | | |
| | B26 | WO 99/59640 A2, A3 | 11-25-1999 | Bracco International B.V. | | |
| | B27 | WO 01/08712 A2, A3 | 02-08-2001 | Epix Medical, Inc. | | |
| | B28 | WO 01/52906 A2, A3 | 07-26-2001 | Epix Medical, Inc. | | |
| | B29 | WO 01/82795 A2, A3 | 11-08-2001 | Research Corporation Technologies | | |
| | B30 * | WO 02/056670 A2 ✓ | 07-25-2002 | The General Hospital | | |
| | B31 | | | | | |
| | B32 | | | | | |

| NON PATENT LITERATURE DOCUMENTS | | | |
|---------------------------------|-----------------------|---|----------------|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ⁴ |
| | C1 | AGUAYO et al., "Nuclear magnetic resonance imaging of a single cell," Nature, Letters to Nature, 07-10-1986, 322:190-191. | |
| | C2 | ALEXANDER, "Design and Synthesis of Macrocyclic Ligands and Their Complexes of Lanthanides and Actinides," Chemical Review, 1995, 95:273-342. | |
| | C3 | BORCH, R.F., et al., "The Cyanohydrinborate Anion as a Selective Reducing Agent," Journal of the American Chemical Society, 06-1971, 93(12):2897-2904. | |
| | C4 | CHO, Z.H., et al., "Some Experiences on a 4 μ m NMR Microscopy," Book of Abstracts, Vol. 1, p.233, Society of Magnetic Resonance in Medicine, 6th Annual Meeting and Exhibition, August 17-21, 1987, New York City, NY., 08-1987, 1:233. | |
| | C5 | COHEN, S.M. et al., "Synthesis and Relaxation Properties of Mixed Gadolinium Hydroxypyridinonate MRI Contrast Agents, Inorganic Chemistry, 2000, 39:5747-5756. | |
| | C6 | GRYNKIEWICZ, G., et al., "A New Generation of Ca ²⁺ Indicators with Greatly Improved Fluorescence Properties," The Journal of Biological Chemistry, 1985, 260(6):3440-3450. | |
| | C7 | HENNESSY, M.J., et al., "NMR Surface Coil Microscopy," Book of Abstracts, Vol. 2, p.461-462, Society of Magnetic Resonance in Medicine, 5th Annual Meeting and Exhibition, August 19-22, 1986, Montreal, Quebec, Canada., 08-1986, 2:461-462. | |

| | | |
|--------------------|-----------------|--|
| Examiner Signature | Date Considered | |
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| | | Application Number | 10/693,252 | | |
| | | Filing Date | October 24, 2003 | | |
| | | First Named Inventor | Meade et al. | | |
| | | Art Unit | 1616 | | |
| | | Examiner Name | To Be Assigned | | |
| | | Attorney Docket Number | A-68448-3 | | |
| Sheet | 5 | of | 6 | | |

| NON PATENT LITERATURE DOCUMENTS | | | |
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| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | |
| | C8 | HOULT, D.I., et al., "The Signal-to-Noise Ratio of the Nuclear Magnetic Resonance Experiment," Journal of Magnetic Resonance, 1976, 24:71-85. | |
| | C9 | HUBIN et al., "Ultra rigid cross-bridged tetraazamacrocycles as ligands- the challenge and the solution," Chemical Communications, 1998, :1675-1676. | |
| | C10 | HUBIN et al., "Crystallographic Characterization of Stepwise Changes In Ligand Conformations as Their Internal Topology Changes and Two Novel Cross-Bridged Tetraazamacrocyclic Copper(II) Complexes," Inorganic Chemistry, 1999, 38:4435-4446. | |
| | C11 | HUBIN et al., "New Iron(II) and Manganese(II) Complexes of Two Ultra-Rigid, Cross-Bridged Tetraazamacrocycles for Catalysis and Biomimicry," Journal of the American Chemical Society, 2000, 122:2515-2522. | |
| | C12 | HUBIN et al., "Topologically Constrained Manganese(III) and Iron(III) Complexes of Two Cross-Bridged Tetraazamacrocycles," Inorganic Chemistry, 2001, 40:435-444. | |
| | C13 | HUBIN et al., "Potentiometric Titrations and Nickel(II) Complexes of Four Topologically Constrained Tetraazamacrocycles," Supramolecular Chemistry, 2001, 13:261-276. | |
| | C14 | JACKELS, "Enhancement Agents for Magnetic Resonance and Ultrasound Imaging. Chapter 20: Enhancement Agents for Magnetic Resonance Imaging: Fundamentals," Pharm. Med. Imag., 1990, 20(3):645-661. | |
| | C15 | JACOBS et al., "Magnetic Resonance Microscopy of Embryonic Cell Lineages and Movements," Science, 1994, 263:681-684. | |
| | C16 | JOHNSON, G.A., et al., "MR Microscopy at 7.0 T," Works in Progress, Society of Magnetic Resonance in Medicine, Sixth Annual Meeting and Exhibition, August 17-21, 1987, New York City, NY, 08-1987, :23. | |
| | C17 | LI et al., "A Calcium-Sensitive Magnetic Resonance Imaging Contrast Agent," Journal of the American Chemical Society, 1999, 121:1413-1414. | |
| | C18 | MEADE, T.J. et al., "Hydrophobic, Regiospecific Guest Binding by Transition-Metal Host Complexes Having Permanent Voids as Revealed by FT-NMR Relaxation Studies," Journal of the American Chemical Society, 1986, 108:1954-1962. | |
| | C19 | MEYER et al., "Advances in Macrocyclic Gadolinium Complexes as Magnetic Resonance Imaging Contrast Agents," Investigative Radiology, 09-1990, 25(1):S53-S55. | |
| | C20 | MOATS et al., "A "Smart" Magnetic Resonance Imaging Agent That Reports on Specific Enzymatic Activity," Agnew Chemical International Edition England, 04-1997, 36(7):726-728. | |
| | C21 | MOI, M.K., et al., "The Peptide Way to Macrocyclic Bifunctional Chelating Agents: Synthesis of 2- (p-Nitrobenzyl) - 1,4,7,10-tetraazacyclododecan- N, N', N'', N'''- tetraacetic Acid and Study of Its Yttrium(III) Complex," Journal of the American Chemical Society, 1988, 110(18):6266-6267. | |
| | C22 | NIJHOF, E.J., et al., "High-Resolution Proton Imaging at 4.7 Tesla," Proceedings of Soc. Magn. Reson. Med., 1987, pg. 925. | |
| | C23 | RUNGE, V.M., et al., "Future directions in magnetic resonance contrast media," Topics in Magnetic Resonance Imaging, 1991, 3(2):85-97. | |
| | C24 | RUSSELL, E.J., et al., "Multicenter Double-Blind Placebo-Controlled Study of Gadopentetate Dimeglumine as an MR Contrast Agent: Evaluation in Patients with Cerebral Lesions," American Journal of Roentgenology, 04-1989, 152:813-823. | |

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| Examiner Signature | | Date Considered | |
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| | | Attorney Docket Number | A-68448-3 |
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| | C25 | SHUKLA et al., "Design of Conformationally Rigid Dimeric MRI Agents," Magnetic Resonance in Medicine, 1996, 36(6):925-931. | |
| | C26 | SILLERUD, L.O., et al., "Proton NMR Microscopy of Intact Multicellular Tumor Spheroids," Book of Abstracts, Vol. 1, p.468, Society of Magnetic Resonance in Medicine, 6th Annual Meeting and Exhibition, August 17-21, 1987, New York City, NY, 08-1987, 1:468. | |
| | C27 | STAUBLI et al., "The Design and Synthesis of Fluorescently Detectable Magnetic Resonance imaging Agents for Embryonic Cell Lineage Analysis," American Chemical Society: Division of Inorganic Chemistry, 209th ACS National Meeting, Anaheim, California. Abstract No. 385 (April 2-6, 1995)., 04-1995. | |
| | C28 | TSIEN, R.Y. "New Calcium Indicators and Buffers with High Selectivity Against Magnesium and Protons: Design, Synthesis, and Properties of Prototype Structures," Biochemistry, 1980, 19(11):2396-2404. | |
| | C29 | TWEEDLE, M.F., et al., "Considerations Involving Paramagnetic Coordination Compounds as Useful NMR Contrast Agents," Nuclear Medicine and Biology, 1988, 15(1):31-36. | |
| | C30 | WEISMAN et al., "Cross-Bridged Cyclam. Protonation and Li+ Complexation in a Diamond-Lattice Cleft," Journal of the American Chemical Society, 1990, 112:8604-8605. | |
| | C31 | WEISMAN et al., "Synthesis and transition-metal complexes of new cross-bridged tetraamine ligands," Chemical Communications, 1996, pp. 947-948. | |
| | C32 | WONG et al., "Synthesis and Characterization of Cross-Bridged Cyclams and Pendant-Armed Derivatives and Structural Studies of Their Copper(II) Complexes," Journal of the American Chemical Society, 2000, 122:10561-10572. | |
| | C33 | | |
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| Examiner Signature |  | Date Considered | 7-7-03 |
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